The “All of Us” Research Program

No potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: Although cardiogenic shock is rare in patients with pheochromocytoma, we agree with Whitelaw et al. that it is important for clinicians to be aware of this possibility, which was recently highlighted in a Case Record of the Massachusetts General Hospital.[1] The cardiomyopathy, whether dilated or hypertrophic, may be completely reversible with tumor resection.[2]

Tassone comments on the role for measurement of serum chromogranin A levels as a case detection test for pheochromocytoma. Chromogranin A is stored and released from dense-core secretory granules of neuroendocrine cells, and levels are elevated in most patients with pheochromocytoma. However, a high chromogranin A level is not specific for pheochromocytoma, and elevations may be seen in patients with other neuroendocrine tumors or with non-neuroendocrine tumors, atrophic gastritis, or pernicious anemia. Elevations may also be seen in patients treated with proton-pump inhibitors and those with impaired hepatic or renal function. Thus, the estimated specificity of a high level of chromogranin A for pheochromocytoma is 50%.[3] For these reasons, we do not recommend measurement of chromogranin A levels as a case detection test for pheochromocytoma.

With regard to Tassone's comment on the clonidine suppression test: it was developed in the early 1980s to address the high false-positive rate for plasma fractionated catecholamines.[4] Clonidine is a centrally acting α2-adrenergic receptor agonist that suppresses the release of catecholamines from neurons but does not affect the secretion of catecholamines by a pheochromocytoma. However, given the advances in laboratory methodology and measurement of fractionated metanephrines in the urine and blood with use of appropriate reference ranges, the clonidine suppression test rarely has a role in the diagnosis of this disease.

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Since publication of their article, the authors report no further potential conflict of interest.

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The "All of Us" Research Program

TO THE EDITOR: Denny and colleagues (Aug. 15 issue)[1] describe the progress of the All of Us Research Program. In Scotland, which has a population of 5.43 million, a patient registry[2] is achieving some of the advantages envisaged by All of Us. The Scottish Health Research Register (SHARE) began accessing data from electronic health records (EHRs) in 2011 and obtaining genomic data (from "leftover" blood samples) in 2013; it now includes data on 270,604 persons who are 11 years of age or older (as of August 2019) and has collected 97,642 blood samples. The means of recruitment include the SHARE website,[3] awareness raising through printed ma-

terials, social media, and radio, and face-to-face contact between paid recruiters and patients in hospitals and clinics. Persons attending health-related events such as the opening of new facilities, conferences, science fairs, open houses, and sports events are also recruited.

Participants agree to be contacted by SHARE to discuss participation in studies for which they meet inclusion criteria as described on the SHARE website. Researchers are then provided with contact details for potential study participants. So far, SHARE has supported 102 studies, including surveys, genetic linkage studies, and trials.

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: The Special Report on the All of Us Research Program outlines many commendable features, including broad representation of populations and engagement of participants in planning. Nonetheless, only a single sentence addresses the failure to include children; it states that "protocols are being developed to enable enrollment."

The failure to include children is a profound scientific flaw, in part because physical and behavioral exposures that occur during childhood (and in utero) determine future health. Other programs in the United States have protocols to enroll children and have enrolled thousands of pregnant women and children in population-based research. This experience could have provided an important framework for All of Us, which could have included children so that risks in childhood would be incorporated from the inception of the program. Instead, these critical early life events are still not being addressed despite the billions of dollars invested. Women and children have long been overlooked in national studies, and the slow pace of bringing them into All of Us means that the most vulnerable members of society are still not counted as "all of us."

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THE AUTHOR AND COLLEAGUES REPLY: We applaud the efforts of the SHARE program described by Sullivan et al. The use of clinical data and biospecimens obtained during clinical visits has proved to be a powerful model in other studies such as those in the Electronic Medical Records and Genomics (eMERGE) Network[1] and the Million Veteran Program.[2] SHARE also allows researchers to recontact participants; this is not usually a feature of biobanks, and it is an important part of All of Us. Collaboration and shared data standards among diverse international cohorts, as envisioned by the International HundredK+ Cohorts Consortium,[3] will be important in the advancement of discovery and health care.

We thank Murray for highlighting the importance of the inclusion of children and pregnant women in All of Us. Indeed, these are underrepresented populations in biomedical research and will be an important part of our program as we aim to study health and disease across the human life span. A total of 3800 pregnant women have enrolled in All of Us, and 6021 participants have shared their pediatric EHR information. All of Us will soon engage in a pilot to offer pregnant women who enroll in the program to also enroll in the PregSource project of the National Institutes of Health,[4] a crowdsourced research project to collect data on maternal, fetal, and infant health. This is a first step in our effort to include data on pregnancy

in the data set. The inclusion of children is crucial to the success of All of Us. We have begun to work on the appropriate policies, protocols, communication methods, and infrastructure necessary to achieve this goal. Because overall recruitment in the All of Us program is still in the early stages, there is ample opportunity to expand to all populations, including children.

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Since publication of his article, Dr. Denny reports no further potential conflict of interest. Drs. Devaney and Gebo report no potential conflict of interest relevant to this letter.

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Letters to the Editor are considered for publication, subject to editing and abridgment, provided they do not contain material that has been submitted or published elsewhere.

Letters accepted for publication will appear in print, on our website at NEJM.org, or both.

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Notices submitted for publication should contain a mailing address and telephone number of a contact person or department. We regret that we are unable to publish all notices received.

HARVARD MEDICAL SCHOOL

The following courses will be offered in Boston: "Update in Internal Medicine 2019" (Dec. 8–14); "Nephrology 2020" (March 15–20); and "Musculoskeletal Ultrasound Hands-on Diagnostics and Guided Interventional Skills with Cadaver Lab" (March 28 and 29). They are jointly presented by Harvard Medical School and Beth Israel Deaconess Medical Center.

Contact the Department of Continuing Education, Harvard Medical School, P.O. Box 825, Boston, MA 02117-0825; or call (617) 384-8600; or e-mail ceprograms@hms.harvard.edu; or see http://updateinternalmedicine.com, http://nephrologyboston.com, or http://cmeregistration.hms.harvard.edu/MSK2020, respectively.

ADVANCED EUROPEAN BIOETHICS COURSE

The course, entitled "Suffering, Death and Palliative Care," will be offered in Nijmegen, the Netherlands, March 24–27. It is presented by the section of Healthcare Ethics, IQ healthcare, Radboud University Medical Centre.

Contact Valesca Hulsman, Radboud University Medical Centre, P.O. Box 9101, 114, 6500 HB Nijmegen, the Netherlands; or call +31 (0)24 3615305; or e-mail valesca.hulsman@radboudumc.nl; or see https://bit.ly/2eqVZ4A.

THOMAS L. PETTY ASPEN LUNG CONFERENCE

The 63rd Annual Meeting, entitled "ARDS in the 21st Century: New Insights into Clinical and Mechanistic Heterogeneity," will be held in Aspen, CO, June 10–13. Deadline for submission of abstracts is Feb. 14.

Contact Dr. Eric Schmidt, c/o Jeanne Cleary, Thomas L. Petty Aspen Lung Conference, P.O. Box 1622, Parker, CO 80134; or call (303) 358-2797; or e-mail Jeanne.Cleary@ucdenver.edu; or see http://www.aspenlungconference.org.

ROOSEVELT ISLAND HISTORICAL SOCIETY

The Roosevelt Island Historical Society is seeking physicians who worked on the New York City island as students, interns, and residents to learn about their experiences. The island was known as Welfare Island until 1973.

Contact Judith Berdy, Roosevelt Island Historical Society, 531 Main St., Roosevelt Island, NY 10044; or call (212) 688-4836; or e-mail rooseveltislandhistory@usa.com.